



Yinzhi Lang, Ph.D.

Research Assistant Professor

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Biographical Sketch

Yinzhi Lang, PhD, is a Research Assistant Professor in the Department of Pharmacotherapy and Translational Research at the UF College of Pharmacy. Dr. Lang completed her PhD program in 2016 from Ocean University of China and worked as a senior Scientist in Shanghai Greenvally Pharmaceutical Co.Ltd between 2016 and 2018. In 2018, Dr. Lang joined the College of Pharmacy at UF as a Postdoc and has received systematic training in antimicrobial pharmacology, pharmacokinetics and pharmacodynamics from Dr. Bulitta and his collaborators. In 2021, Dr. Lang was appointed as a Research Assistant Professor at UF. Her current research focus on elucidating the mechanisms of drug action and resistance via the latest mass spectrometry (**MS**)-based technology and Quantitative & Systems Pharmacology (**QSP**) modeling approach.

Dr. Lang has over 11 years of experience working with identification and quantification of biological endogenous molecules using liquid chromatography with tandem mass spectrometry (**LC-MS/MS**)-based approaches. This includes the in-depth component and structural analysis of polysaccharides, oligosaccharides, glycoproteins, and glycolipids from marine algae, human milk, animal meat byproducts and microbial cells. For the pharmaceutical compounds, she has created a series of novel UPLC-MS/MS assays to quantify the target site penetration of various classes of antibiotics in Gram-negative bacteria and the intracellular accumulation of antiviral nucleosides/nucleotides analogs in mammalian cells. Further, she has significantly contributed to the development of advanced QSP models, which can integrate the experimental mechanistic data with pathogen killing and resistance to rationally optimize anti-infective therapy. Moreover, she has extensive experience in pharmacokinetics and pharmacodynamics analysis of anti-infectives in *in vitro* and mouse infection models. Dr. Lang is leading and co-leading multiple federal funded anti-infective pharmacology research programs to create novel insights to combat serious infections.

Publications from PhD (as of 8/23/2021)

Published

Peer-reviewed research papers	28
All papers	31
Patents	1
International conference abstracts	67
Ongoing and Completed Research Projects (Role: PD/PI or Co-I)	7
Grant Application – Under Review (Role: Co-I)	4

Pubmed Bibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/1tsW5pHvXgA5I/bibliography/public/?sortBy=pubDate&sdirection=descending>

CURRICULUM VITAE

Yinzhi Lang, Ph.D.

Education

9/2011 to 6/2016

Ph.D. in Medicinal Chemistry School of Medicine and Pharmacy, Ocean University of China, Qingdao, Shandong, China. Advisor: *Dr. Guangli Yu*.

Thesis title: Development and application of LC/MS-based methods for the analysis of human milk glycome:

- Developing novel semi-preparative HPLC methods to achieve 26 purified isobaric oligosaccharides from human milk samples, and characterizing their chain structures in-depth by ESI-CID/HCD-MS/MS.
- Developing a novel combination strategy of glycan labeling and LC-MS/MS for rapid and reliable compositional profiling analysis of human milk oligosaccharides (HMOs, ~200 diverse structures).
- Developing an integrated design for simultaneously isolating and profiling analysis of five types of glycans and glycoconjugates, including HMOs, *N/O*-glycans from glycoproteins, glycosaminoglycans from proteoglycans, and glycolipids.
- Characterizing the expression dynamics of glycans associated with different lactation stages to support future research on optimizing infant formula design.

Preparation and characterization of glycoconjugates from IRA rabbit meat byproducts and sea cucumber:

- Extraction, isolation and identification of chondroitin sulfate C and chondroitin sulfate A (Mw: 13~59 kDa) from IRA rabbit meat byproducts (lungs and ear cartilages) by preparative LC, HPLC and NMR.
- Extraction, isolation and structural characterization of novel O-glycan containing mucins from IRA rabbit intestines by offline ESI-MS/MS.
- Extraction, isolation and structural characterization of novel fucosylated chondroitin sulfates (Mw: 2~30 kDa) from sea cucumber by a combination of enzymatic extraction, preparative LC separation, NMR analysis, and bottom-up analyses using ESI-MS/MS to characterize their degraded oligosaccharides as well as using GC-EI-MS/MS to characterize their methylated derivatives.

9/2007 to 6/2011

B.S. in Pharmacy – School of Pharmacy, Yantai University, Yantai, Shandong, China.

Work experience

Since 8/2021

Research Assistant Professor – Department of Pharmacotherapy and Translational Research, College of Pharmacy (COP), University of Florida (UF), Orlando, FL.

- Applied a series of our novel established UPLC-MS/MS assays to quantify the target site penetration of various beta-lactams, beta-lactamase inhibitors and aminoglycosides in multi-drug resistant bacteria. Together with Dr. Bulitta, formed an auxiliary on UPLC-MS/MS-related analyses of target site penetration determinations. Analyzed and interpreted the penetration data, accumulation data, the hollow fiber *in vitro* infection (HFIM) model data and murine model data using translational Quantitative and Systems Pharmacology (QSP) modeling and Monte Carlo simulations, together with Dr. Jurgen Bulitta and our other collaborators.
- Determination of tobramycin concentrations in plasma and tracheal aspirate of pediatric patients using latest LC-MS/MS to generate novel and urgently needed data to optimize tobramycin-based therapy for pediatric patients. (Collaboration with Dr. Erik A. Jensen, the Children's Hospital of Philadelphia, Philadelphia, PA).
- Optimizing and employing the UPLC-MS/MS methods to assess the *in vitro* membrane permeability, cell uptake and lysosomal sequestration of 11 inhaled drugs in healthy bronchial and alveolar epithelial cell models. These *in vitro* data will significantly contribute to the PBPK modeling analyses which are urgently needed to understand and predict pulmonary absorption and tissue retention of inhaled drugs. (Collaboration with Dr. Rodrigo Cristofolletti, UF-COP, Orlando, FL)

- Optimizing novel assays to determine the outer membrane permeability of β -lactams and β -lactamase inhibitors as well as the intracellular accumulation of aminoglycosides in resistant *K. pneumoniae* strains to inform rationally optimized dosage regimens (Collaboration with Dr. Zackery Bulman, University of Illinois at Chicago, Chicago, IL.)
- Employing latest intracellular target site penetration and receptor binding assays of anti-*M. tuberculosis* agents to provide the mechanistic basis for rational optimization of dosage regimens to generate novel and urgently needed data to optimize antibiotic combination therapies that can successfully combat *M. tuberculosis*. (Collaboration with Dr. George L. Drusano, UF-COM, Orlando, FL)
- Developing and rationally optimizing orally administered dosage regimens of novel β -lactam and tarocin combinations against methicillin susceptible and methicillin resistant staphylococci via QSP modeling. (Collaboration with Dr. Terry Roemer, Prokaryotics, INC. New Jersey, NJ)
- Comprehensive stability analysis of 13 β -lactam and β -lactamase inhibitors, and novel in vitro supplement dosing strategy to mitigate thermal drug degradation.
- Determining and optimizing combination dosage strategies that can successfully combat SARS-CoV-2, based on mechanistic target site concentration assays, and dynamic *in vitro* infection models. (Collaboration with Dr. George L. Drusano and Dr. Ashley N. Brown, UF-COM, Orlando, FL)
- Exploring the β -lactam structure-penetration relationships via computational chemistry and multivariate data analysis to identify rapid penetrating antibiotic structure features.
- Creating a series of UPLC-MS/MS assays to analyze the pharmacokinetic profiles of various antibacterial or antiviral agents in the HFIM and murine models.
- Population Pharmacokinetics of Enrofloxacin and Florfenicol in the Giant Danio (*Devario aequipinnatus*) Following Oral Administration of Both Antibiotics and Bath Administration of Enrofloxacin. (Collaboration with Dr. Roy Yanong, UF-IFAS, Ruskin, FL)
- Translational mathematical modeling analyses to describe the time-course of the effects of bacterial membranes on the activation of natural killer cells. (Collaboration with Dr. Alicja Copik, UCF College of Medicine, Orlando, FL)
- Distinguishing inducible and non-inducible resistance to colistin in *Pseudomonas aeruginosa* by Quantitative and Systems Pharmacology modeling at low and standard inocula.
- Characterization of aminoglycoside penetration into human lung epithelial lining fluid via population pharmacokinetics.

10/2018 to 7/2021

Postdoc – Department of Pharmacotherapy and Translational Research, College of Pharmacy (COP), University of Florida (UF), Orlando, FL. *Mentor: Dr. Jürgen B. Bulitta*

- Developing innovative assays that accounts for time-dependent release of β -lactamase enzymes to precisely determine the outer membrane permeability of β -lactams in resistant *A. baumannii* strains.
- Creating UPLC-MS/MS data for multiple antibiotic classes to validate their PK target concentrations in hollow fiber infection model (Collaboration with Dr. Cornelia Landersdorfer, Monash University, Melbourne, Victoria, Australia)
- Population pharmacokinetic modeling, Monte Carlo simulations and optimal study design for enrofloxacin and florfenicol in the giant danio (*Devario aequipinnatus*) following oral and bath administration (Collaboration with Dr. Roy P.E. Yanong, UF-IFAS, Tampa, FL).
- Characterizing the outer membrane permeability of 6 β -lactams to combat *New Delhi Metallo- β -lactamase* and CTX-*M*-Co-producing *Klebsiella pneumoniae* (KP). (Collaboration with Dr. Brian Tsuji, Buffalo, NY)
- Developing novel UPLC-MS/MS assays to characterize the intracellular penetration and accumulation of antiviral agents (galidesivir, favipiravir, Merck EIDD-1931, and remdesivir) and their active neo-nucleotide triphosphate metabolites. Developing QSP modeling to characterize the metabolism pathways and optimize therapy regimens, to combat SARS-

CoV-2. (Collaboration with Dr. George L. Drusano and Dr. Ashley N. Brown, UF-COM, Orlando, FL)

- Developing novel UPLC-MS/MS assays to characterize the intracellular penetration and accumulation of anti-cancer agents (cytarabine) and the biosynthesis of its active neo-nucleotide triphosphate metabolites (collaboration with Dr. Jatinder Lamba, UF-COP, Gainesville)
- Determination of gentamicin, amikacin, ceftazidime and avibactam concentrations in hollow fiber infection model to validate their PK target concentrations (Collaboration with Dr. Zackery Bulman, University of Illinois at Chicago, Chicago, IL).

- 4/2018 to 8/2018 **Postdoc** – College of Veterinary Medicine, Mississippi State University, Mississippi State, MS, United States. Supervisor: *Prof. Dr. Xiufeng Wan*.
- Building an efficient workflow for influenza viral glycoproteomics to provide mechanistic data for the interactions between influenza cell and host tropisms.
- 7/2016 to 2/2018 **Scientist II** –Shanghai Greenvalley Pharmaceutical CO. Ltd., Shanghai, China. R&D of the GV-971 for treatment Alzheimer’s disease (AD), phase III clinical study:
- Developing instrumental analysis methods (GC-MS, CE-MS, LC-MS) for QC and ADME study of an innovative anti-AD agent GV-971 (Phase III, NCT04520412).
 - Establishing nano-LC-MS/MS based proteomics platform to discover clinical diagnostic biomarkers of AD.
 - Exploring the ‘microbiota-gut-brain axis’ theory to elucidate novel pharmacological mechanisms of GV-971 for treating AD.
- 3/2013 to 9/2013 **Research Intern** – China Kangda Food Chemistry CO. Ltd., Qingdao, Shandong, China
- Extraction and characterization of chondroitin sulfates and mucins from IRA rabbit meat byproducts.

Teaching

- 2023 Spring Teacher for **UF PHA6133 [Translational Clinical Pharmacology] course** led/coordinated by Dr. Jürgen Bulitta in the spring of 2023, Department of Pharmacotherapy and Translational Research, COP, UF.
Lecture: translational drug development in action-experimental approaches for antibiotics
- Provided Ph.D. students with an in-depth understanding of non-clinical experimental and mathematical modeling methodologies as well as their applications to rationally optimize novel combination dosing strategies against bacterial ‘superbugs’.
- 2022 Fall Laboratory studies **training – Basic and advanced UPLC-MS/MS based techniques**, Department of Pharmacotherapy and Translational Research, COP, UF.
- Principles of UPLC and ESI-MSⁿ for separating, structural elucidation and quantification of various types of compounds.
 - Basic and advanced sample handling methods for enhanced analysis of analytes with different structure features and from different matrices.
- 2021 Spring Full Course Teaching Assistant – **Translational Clinical Pharmacology**. Department of Pharmacotherapy and Translational Research, COP, UF.
- Concepts and Principles of PKPD In vitro (IVIVC) → animal → human scaling
 - Basic Modeling Methods and Study Design Empiric and Mechanistic Models for Translational Analyses Population Modeling Methods & Software Achieving Patient Target Goals Precisely Translational Drug Development in Action

Peer-Reviews

- Since 2022 Reviewer for six MDPI journals.
- Reviewed 3 manuscripts for *International Journal of Molecular Sciences*
 - Reviewed 2 manuscripts for *Marine Drugs*

- Reviewed 4 manuscripts for *Molecules*
- Reviewed 2 manuscript for *Biomedicines*
- Reviewed 1 manuscript for *Antibodies*
- Reviewed 1 manuscript for *Pathogens*

Research interests

Translational and Clinical Pharmacology, Treatment for infectious diseases, Quantitative and Systems Pharmacology (**QSP**) modeling, Pharmacokinetics/Pharmacodynamics (**PK/PD**) modeling, Research and development (**R&D**) of anti-infective drugs, Neurodegenerative diseases, Infant formula design, LC/MS-based omics to elucidate relationships between microbe and host systems.

Honors and awards

10/2015	Excellent Post-graduate Direct Scholarship, Ocean University of China
09/2014	University Scholarship, First prize, Ocean University of China
09/2012	University Scholarship, First prize, Ocean University of China
10/2010	University Scholarship, Second prize, Yantai University
10/2009	University Scholarship, First prize, Yantai University
10/2008	University Scholarship, First prize, Yantai University

Researching skills

- **13 years** of experience in state-of-the-art LC/MS-based analyses, including Agilent 1260, Agilent 1290 (Agilent), Acquity I-Class UPLC system (Waters), LTQ Orbitrap XL, LTQ Orbitrap Fusion, LTQ Orbitrap Fusion / Q Extractive high-resolution mass spectrum (Thermo-Fisher Scientific), SCIEX Q-trap 6500+ (MRM) (AB SCIEX) and Q-TOF (Agilent).
- **5 years** of experience in developing QSP, PK/PD modeling in anti-infective pharmacology field.
- Highly proficient in a large array of modeling, simulation and statistical analysis, software packages (including S-ADAPT-TRAN, NONMEM, MONOLIX, Phoenix WinNonLin, R, Shiny, NLMIXR, Berkeley Madonna, SPSS, XLSTAT, SIMCA & GraphPad Prism).
- Highly proficient in a large array of structural characterization, identification and quantification software packages (including FTIR, MestReNova, DeconTools, GlycoResoft, GlycoWorkbench, PMi-Byonic, Proteome Discoverer, Skyline-daily, Scaffold, Thermo Fisher Scientific Xcalibur™, AB Sciex Analyst®, and Agilent MassHunter)
- Extensive experience in measuring microbial & mammalian intracellular drugs and metabolites
- Extensive experience in membrane permeability and intracellular drug accumulation studies
- Extensive experience in LC-MS/MS based proteomics, glycomics and glycoproteomics studies.
- Extensive experience in qualification and quantification of large macromolecules using bottom-up combination strategies of chemical/enzymatical degradation, derivatization, and LC-MS/MS.
- Extensive experience in extraction, semi-preparative purification and in-depth characterization of unknown compounds using LC, HPLC, FTIR, NMR, and MS/MS technologies.
- Programming skills: Certificated by National Computer Rank Examination (NCRE) (China): **Visual C++ (Rank II) Certificate** and **Internet technology (Rank III) Certificate**.
- Highly proficient in literature searching and management (Endnote & Notepress)
- Teaching assistant for course **PHA6133**, "Translational Clinical Pharmacology"

Professional memberships

American Society for Microbiology (ASM); International Society for Pharmacometrics (IsoP); European Society of Clinical Microbiology and Infectious Diseases (ESCMID)

EXECUTIVE SUMMARY

Funding	Total (since 2018)
4 Grants application - under review (Role: Co-Investigator)	\$21,493,792
5 Active grants / contracts - ongoing	\$9,948,931
1 Active grants / contracts (Role: Principal Investigator)	\$60,279
4 Active grants (Role: Co-Investigator)	\$9,888,652
2 Completed grants / contracts	\$90,000
1 grant as Principal Investigator or PD/PI	\$70,000
1 grant as Co-Investigator	\$20,000
4 Grants – not awarded (Role: Co-Investigator)	\$39,489,114
Participated 6 grants when was Postdoc	\$14,103,000

Publications	Total (since 2014)
All papers	31
Peer-reviewed papers & book chapters	28
Original research papers	24
Review papers	3
Patents	1
International/National conference abstracts/posters	67
Invited workshop lectures	2

RESEARCH GRANTS**GRANT APPLICATIONS – Under Review**

Bulitta JB (PD/PI), Cristofolletti R (Co-I), **Lang Y (Co-I)**, Sayed A (Co-I)
 Characterizing antibiotic efficacy via latest hollow fiber infection models and organs on a chip
 NIH/NIAID NIHA175N93023R00003 (5/23) Program: “Pre-Clinical Models of Infectious Diseases”
 06/03/2024 – 06/02/2025, \$2,370,587

Drusano GL (co-equal multi PD/PI [contact]; PD/PI Project 2 and Amin Core), Bulitta JB (co-equal multi PD/PI [non-contact]; PD/PI Project 1; Co-I Admin Core), Louie A (PD/PI Project 3), **Lang Y (Mechanistic Assay Core Lead, Co-I of Project 1)**, Neely MN (Mathematical Modeling Core Lead), Boyce JD (Co-I), Schweizer HP (Co-I), Ropy Sayed A (Co-I), Lee RE (Co-I), Copik A (Co-I), Basso KB (Co I), Bonomo RA (Co-I), Balasubramanian V (Other)

Translational development of new agents alone and in combination to combat Gram-negative pathogens important in Ventilator- Associated Bacterial Pneumonia: Leveraging the Gram-negative toolbox that is ready for prime time
 National Institutes of Health, NIH / NIAID, P01 for PAR-22-225; Impact scored of 30
 1/1/2024 – 12/31/2028, \$11,817,521

Bulitta JB (PD/PI), Drusano GL (Co-I), **Lang Y (Co-I)**, Louie A (Co-I), Boyce J (Co-I), Bonomo R (Co-I), Lee R (Co-I).
 Mechanistically optimized beta-lactam combination dosing strategies to combat resistant Klebsiella pneumoniae.
 National Institutes of Health, **NIH / NIAID**, R01 for PA-20-185; Scored a **30th percentile**
 07/01/2023 – 06/30/2028, \$3,743,664

Copik A (PD/PI, Contact), Altomare D (PD/PI), Bulitta JB (Co-I), **Lang Y (Co-I)**.
 Bacterial vesicles for stimulation of innate immunity to treat cancer.
 National Institutes of Health, **NIH / NCI**, R01 for PA-22-085 (Microbial-based Cancer Imaging and Therapy - Bugs as Drugs)
 07/01/2023 – 06/30/2028, \$3,562,020

ONGOING PROJECTS – Awarded**1. Lang Y (PD/PI), Bulitta J (Co-I)**

Determination of tobramycin concentrations in plasma and tracheal aspirate of pediatric patients using latest LC-MS/MS

National Institutes of Health, NIH, 1R34HL155690 – **Philadelphia Children's Hospital Subcontract**

03/01/2022 – 07/31/2024, \$60,279 (UF subaward)

2. Drusano GL (PD/PI), Louie A (Co-I), Bulitta JB (Co-I), Lang Y (Co-I), Kim S (Co-I), Neely M (Co-I), Prideaux B (Co-I)

Optimizing Multi-drug *Mycobacterium tuberculosis* Therapy for Rapid Sterilization and Resistance Suppression

National Institutes of Health, **NIH / NIAID**, PA-20-185

12/01/2022 – 11/30/2027, \$6,627,424

3. Bulman ZP (PD/PI), Mankin A (Co-I), Bulitta JB (Co-I), Lang Y (Co-I), Li J (Co-I), Hauser AR (Co-I), Ozer EA (Co-I)

Precise Combination Strategies Targeting Carbapenem-Resistant *Klebsiella pneumoniae*

National Institutes of Health, **NIH / NIAID**, PA-20-185

09/01/2022 – 08/31/2027, \$3,756,365 (\$602,036 UF-subaward)

4. Cristofolletti R (PD/PI), Hochhaus G (Co-I), Bulitta JB (Co-I), Lang Y (Co-I), Mullin J (Co-I), Le Merdy M (Co-I), AlQaraghuli F (Co-I), Lukacova V (Co-I).

Advancing *in vitro* and (patho)physiology-based pharmacokinetics models to understand and predict pulmonary absorption and tissue retention of inhaled drugs.

U.S. Food and Drug Administration, **FDA**, 75F40122C00182.

09/30/2022 – 09/29/2025, \$1,844,289.

5. Roemer T (PD/PI), Louie A (UF-subaward PI), Bulitta JB (Co-I), Lang Y (Co-I), Drusano (GL)

SBIR: Prokaryotics SBIR Phase 2b.

Development of a PO-administered beta-lactam-tarocin combination agent to treat methicillin susceptible and methicillin resistant staphylococci.

National Institutes of Health, **NIH / NIAID**, R44AI136213

7/1/2022 – 6/30/2025, \$814,903 (UF-subaward)

6. Tsuji BT (PD/PI), Bulitta JB (PD/PI), Louie A (Co-I), Moya B (Co-I), Drusano GL (Co-I), Chen L (Co-I), Kreiswirth BN (Co-I), Bulman ZP (Co-I)

Novel Strategies for Antibiotic Combinations to Combat Gram-negative Superbugs

National Institutes of Health, **NIH / NIAID**, 1R01AI148560-01

12/20/2019 – 11/30/2024, \$3,920,000

Role: Postdoc named on grant application.

7. Bulitta JB (PI), Lee RE (Co-I), Schweizer HP (Co-I), Louie A (Co-I), Moya B (Co-I), Drusano GL (Co-I), Basso KB (Co-I), Copik A (Co-I), Bonomo R (Co-I), Balasubramanian V (Co-I)

Combating resistant superbugs by understanding the molecular determinants of target site penetration and binding

National Institutes of Health, **NIH / NIAID**, 1R01 AI136803-01

8/10/2018 – 7/31/2023, \$5,728,000

Role: Postdoc

COMPLETED PROJECTS**8. Bulitta JB (PI), Louie A (Co-I), Boyce JD (Co-I), Bonomo R (Co-I), Drusano GL (Co-I)**

Next-generation combination dosing strategies to combat resistant *Acinetobacter baumannii*

National Institutes of Health, **NIH / NIAID**, 1R01AI130185-01,

11/08/2017 – 10/31/2022, \$3,409,000

Role: Postdoc

9. Bulitta JB (PD/PI), Lang Y (PD/PI)

Supporting antimicrobial target site penetration research

Curza, Donation, 2022, \$70,000

10. Bulitta JB (PD/PI), Lang Y (Co-I)

First characterization of antibiotic target site penetration and receptor binding by β -lactam antibiotics in *Mycobacterium tuberculosis*

UF College of Pharmacy, Research Enhancement, PROSPER Seed / Pilot Funding
7/1/2021 – 1/31/2022, \$20,000

11. Bulitta JB, Jiao Y, **Lang Y**, Zhou J.

Developing innovative therapeutic strategies to combating Sars-CoV-2.

UF Clinical and Translational Science Institute, UF-CTSI, seed funding grant.
4/1/2020 – 12/31/2020, \$50,000

Role: Postdoc named on grant

12. Luna BM (PI), Spellberg B, **Bulitta JB (Sub-award PI)**, Louie A, Drusano GL, and Robert Bonomo
A Preclinical Mouse Model of *Acinetobacter baumannii* Infection for Antibacterial Development

U.S. Food and Drug Administration, **FDA**, BAA-17-00123, HHSF223201710199C
9/25/2017 – 12/31/2021, \$996,000 (UF-subaward)

Role: Postdoc

Major Peer-Reviewed Grant Applications – Not Awarded

13. Bulitta JB (PD/PI, Contact), Purcell B (PD/PI), Heine H (Co-I), **Lang Y (Co-I)**, Louie A (Co-I), Drusano GL (Co-I).

Creating a prototype platform for the rational use of efficacious oral and intravenous double β -lactam antibiotic combinations that can combat resistant pathogens.

Medical CBRN Defense Consortium, **MCDC**, RPP-22-11, objective area: Treatment (TRE-22-11): Therapeutic Medical Countermeasure Strategies for Addressing Emerging Bacterial Threats
01/01/2023 – 12/31/2027, \$16,276,294. (Enhanced White Paper, *Applied in 2022*)

14. Bulitta JB (PD/PI, Contact), Purcell B (PD/PI), Heine H (Co-I), **Lang Y (Co-I)**, Louie A (Co-I), Drusano GL (Co-I).

Reinvigorating old antibiotics in efficacious combination therapies.

Medical CBRN Defense Consortium, **MCDC**, RPP-22-10: objective area: ReVAMP: ReinVigorating Abandoned AntiMicrobial Products – Novel Broad Spectrum Antibacterial Medical Countermeasures (MCM) for Treatment of Biothreat Bacterial Infections
01/01/2023 – 12/31/2027, \$18,802,044. (Enhanced White Paper, *Applied in 2022*)

15. Bulman ZP (PD/PI), Mankin A (Co-I), Bulitta JB (Co-I), **Lang Y (Co-I)**, Li J (Co-I), Hauser AR (Co-I), Ozer EA (Co-I)

Targeting Carbapenem-Resistant *Klebsiella pneumoniae* with Molecularly Precise Combination Strategies
National Institutes of Health, NIH / NIAID

11/1/2021 – 9/30/2026, \$3,772,557 (\$606,000 UF-subaward, *Applied in 2021*)

16. Brown A, Drusano GL (Co-I), Bulitta JB (Co-I), **Lang Y (Co-I)**, Tuanyok A (Co-I)

Optimizing combination therapy for COVID-19

National Institutes of Health, **NIH / NIAID**, R01 for PA-20-185
09/01/2022 – 08/31/2027, \$3,804,776. (*Applied in 2021*)

PUBLICATIONS

PubMed Bibliography

<https://www.ncbi.nlm.nih.gov/myncbi/1tsW5pHvXgA5l/bibliography/public/?sortby=pubDate&sdirection=descending>

Google Scholar Citations: https://scholar.google.com/citations?user=Ai5_bQkAAAAJ&hl=en

Web of Science Researcher: <https://www.webofscience.com/wos/author/record/GLU-8044-2022>

ResearchGate: <https://www.researchgate.net/profile/Yinzhi-Lang/research>

Orcid: <https://orcid.org/0000-0002-6857-4516>

Full Papers Published

1. Zhou J, Qian Y, **Lang Y**, Zhang Y, Tao X, Moya B, Sayed ARM, Landersdorfer CB, Shin E, Werkman C, Smith NM, Kim TH, Kumaraswamy M, Shin BS, Tsuji BT, Lee R, Bulitta JB. Comprehensive stability analysis of 13 β -lactam and β -lactamase inhibitors, and novel in vitro supplement dosing strategy to mitigate thermal drug degradation. *Antimicrob Agents Chemother*. Accepted Jan 6, 2024.
2. Shin E, Zhang Y, Zhou J, **Lang Y**, Sayed ARM, Werkman C, Jiao Y, Kumaraswamy M, Bulman Z, Luna BM, Bulitta JB. Improved characterization of aminoglycoside penetration into human lung epithelial lining fluid via population pharmacokinetics. *Antimicrob Agents Chemother*. 2024 Jan 3:e0139323. [PMID: 38169309](#).
3. Bulitta JB, Shin E, Bergen PJ, **Lang Y**, Forrest A, Tsuji BT, Moya B, Li J, Nation RL, Landersdorfer CB. Distinguishing inducible and non-inducible resistance to colistin in *Pseudomonas aeruginosa* by Quantitative and Systems Pharmacology modeling at low and standard inocula. *J Pharm Sci* 2023. S0022-3549(23)00437-9. [PMID: 37879409](#)
4. Vorbach BS, Zhou J, **Lang Y**, Bulitta JB, Yanong RPE. Population Pharmacokinetics of Enrofloxacin and Florfenicol in the Giant Danio (*Devario aequipinnatus*) Following Oral Administration of Both Antibiotics and Bath Administration of Enrofloxacin. *Aquaculture* 2024. 579: 740222. [Link](#)
5. Agyeman AA, López-Causapé C, Rogers KE, Lucas DD, Cortés-Lara S, Gomis-Font MA, Fraile-Ribot P, Figuerola J, **Lang Y**, Franklyn ERT, Lee WL, Zhou J, Zhang Y, Bulitta JB, Boyce JD, Nation RL, Oliver A, Landersdorfer CB. Ceftolozane/tazobactam plus tobramycin against free-floating and biofilm bacteria of hypermutable *Pseudomonas aeruginosa* epidemic strains: resistance mechanisms and synergistic activity: Running title: Ceftolozane/tazobactam plus tobramycin against *Pseudomonas* biofilm. *Int J Antimicrob Agents*. 2023 Jun 12:106887. [PMID: 37315906](#).
6. Tait JR, Harper M, Cortés-Lara S, Rogers KE, López-Causapé C, Smallman TR, **Lang Y**, Lee WL, Zhou J, Bulitta JB, Nation RL, Boyce JD, Oliver A, Landersdorfer CB. Ceftolozane-Tazobactam against *Pseudomonas aeruginosa* Cystic Fibrosis Clinical Isolates in the Hollow-Fiber Infection Model: Challenges Imposed by Hypermutability and Heteroresistance. *Antimicrob Agents Chemother*. 2023 Jul 10:e0041423. [PMID: 37428034](#).
7. Brown AN, **Lang Y**, Zhou J, Franco EJ, Hanrahan KC, Bulitta JB, Drusano GL. Why Molnupiravir Fails in Hospitalized Patients. *mBio*. 2022 Nov 14: e0291622. [PMID: 36374076](#).
8. Smith NM, Boissonneault KR, Chen L, Petraitis V, Petraitiene R, Tao X, Zhou J, **Lang Y**, Kavaliauskas P, Bulman ZP, Holden PN, Cha R, Bulitta JB, Kreiswirth BN, Walsh TJ, Tsuji BT. Mechanistic Insights to Combating NDM- and CTX-M-Coproducing *Klebsiella pneumoniae* by Targeting Cell Wall Synthesis and Outer Membrane Integrity. *Antimicrob Agents Chemother*. 2022 Aug 4: e0052722. [PMID: 35924913](#).
9. Bilal H, Tait JR, **Lang Y**, Zhou J, Bergen PJ, Peleg AY, Bulitta JB, Oliver A, Nation RL, Landersdorfer CB. Simulated Intravenous versus Inhaled Tobramycin with or without Intravenous Ceftazidime Evaluated against Hypermutable *Pseudomonas aeruginosa* via a Dynamic Biofilm Model and Mechanism-Based Modeling. *Antimicrob Agents Chemother*. 2022 Mar 15; 66: e0220321. [PMID: 35041509](#).
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Full Papers Submitted

29. Jiao Y, Bulitta JB#, Kinzig M, Landersdorfer CB, Tao X, **Lang Y**, Zhou J, Moya B, Höhl R, Holzgrabe U, Stephan U, Sörgel F# (#: joint corresponding authors). Comparable Renal Secretion and Reabsorption of

Ciprofloxacin in Patients with Cystic Fibrosis and Healthy Volunteers assessed via Population Pharmacokinetics. Submitted.

30. Kaur JN, Singh N, Smith N, Klem J, Cha R, **Lang Y**, Chen L, Kreiswirth B, Holden P, Bulitta JB, Tsuji BT. 2023. Next generation beta-lactam combinations to combat persisters: Harnessing imipenem to curb carbapenem resistance in metallo- β -lactamase-producing *Klebsiella pneumoniae*. mBio. Submitted

Patent

1. Yu G, Zhang Y, Zhu H, **Lang Y**, Zhao X. Method for preparing high-purity chondroitin sulfate A from rabbit ear cartilage. Chinese Patent. CN103788231A.

Invited Workshop Lectures:

1. Bulitta JB, **Lang Y**, Shin E. Phoenix WinNonlin – the Swiss Army Knife of Pharmacokinetics and Pharmacodynamics. SUNY at Buffalo, Buffalo, NY, USA, October 22, 2021.
2. **Lang Y**, Bulitta JB. Development of Tools for Gram-Negative Antibiotic Discovery. National Institute of Allergy and Infectious Disease, Maryland, USA, August 8-9, 2022.

International Conference Presentations

1. Sayed AR, Elsayed AAS, Moya B, Cadet KC, Jimenez-Nieves RH, Shin E, Moya B, **Lang Y**, Zhou J, Zhang Y, Werkman C, Tsuji BT, Drusano GL, Bulitta JB. Time-course of whole-cell Penicillin-Binding Protein (PBP) binding and morphological alterations by eleven β -lactam antibiotics in *Klebsiella pneumoniae* (KP). ASM Microbe. Houston, TX. Jun 15-19, 2023.
2. Werkman C, Oyer JL, Shah NR, Megroz M, Deveson Lucas D, Moya B, Sayed AR, Elsayed AAS, Wright A, Sutaria DS, Tao X, **Lang Y**, Zhou J, Shin E, Landersdorfer CB, Jimenez-Nieves RH, Cadet KC, Jiao Y, Copik AJ, Bonomo RA, Louie A, Drusano GL, Boyce JD, Bulitta JB. Quantifying β -lactam penetration by flow cytometry and confocal microscopy in a double β -lactamase and double efflux pump knockout strain of *Acinetobacter baumannii* (AB). ASM Microbe. Houston, TX. Jun 15-19, 2023.
3. Shin E, Sayed AR, **Lang Y**, Zhou J, Oyer JL, Moya B, Elsayed AAS, Sutaria DS, Shah NR, Werkman C, Jimenez-Nieves RH, Cadet KC, Tao X, Jiao Y, Copik AJ, Bonomo RA, Schweizer HP, Lee RE, Boyce JD, Tsuji BT, Drusano GL, Bulitta JB. Next-generation Quantitative and Systems Pharmacology Modeling of Synergistic Penicillin-Binding Protein (PBP) occupancy patterns in *Klebsiella pneumoniae* (KP). ASM Microbe. Houston, TX. Jun 15-19, 2023.
4. Zhou J, **Lang Y**, Zhang Y, Sayed AR, Shin E, Werkman C, Louie A, Tsuji BT, Bulman ZP, Drusano GL, Bulitta JB. Intracellular accumulation and washout kinetics of three aminoglycosides (AGS) in a highly AGS-resistant *Klebsiella pneumoniae* with a 16S rRNA methyltransferase. ASM Microbe. Houston, TX. Jun 15-19, 2023.
5. **Lang Y**, Zhang Y, Zhou J, Myrick JR, Sayed AR, Elsayed A, Werkman C, Shin E, Cadet KC, Jimenez-Nieves RH, Louie A, Drusano GL, Bulitta JB. Combating *Mycobacterium tuberculosis* (Mtb) by mechanistic insights from a highly sensitive UPLC-MS/MS assay for the parent and M2 metabolite of bedaquiline associated with Mtb and their impact on mycobacterial energy metabolites. 33rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID). Copenhagen, Denmark. Apr 15-18, 2023.
6. Shin E, Sayed AR, **Lang Y**, Zhang Y, Zhou J, Oyer JL, Moya B, Elsayed A, Sutaria DS, Shah NR, Werkman C, Jimenez-Nieves RH, Cadet KC, Tao X, Jiao Y, Copik AJ, Bonomo RA, Schweizer HP, Lee RE, Boyce JD, Louie A, Tsuji BT, Barth AL, Zavascki AP, Drusano GL, Bulitta JB. Synergistic penicillin-binding protein (PBP) occupancy patterns in *Klebsiella pneumoniae* (KP) prospectively validated in a dynamic in vitro hollow fiber infection model. 33rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID). Copenhagen, Denmark. Apr 15-18, 2023.
7. Werkman C, Shah NR, Megroz M, Oyer JL, Deveson Lucas D, Moya B, Sayed AR, Elsayed A, Wright A, Sutaria DS, Tao X, **Lang Y**, Zhang Y, Zhou J, Shin E, Landersdorfer C, Jimenez-Nieves RH, Cadet K, Jiao Y, Copik AJ, Bonomo RA, Louie A, Drusano GL, Boyce JD, Bulitta JB. Synergistic killing of *Acinetobacter*

- baumannii (AB) elicited by simultaneous inactivation of three or all four Penicillin-Binding Proteins (PBPs) among PBP1a, 1b, 2 and 3. 33rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID). Copenhagen, Denmark. Apr 15-18, 2023.
8. Zhang Y, **Lang Y**, Zhou J, Tao X, Sayed AR, Shin E, Werkman C, Smith NM, Tsuji BT, Bulitta JB. Periplasmic target site penetration rates of four β -lactamase inhibitors in *Klebsiella pneumoniae* carbapenemase-2 (KPC-2) producing *Klebsiella pneumoniae*. 33rd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID). Copenhagen, Denmark. Apr 15-18, 2023.
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 13. Zhang Y, **Lang Y**, Zhou J, Tao X, Sayed A, Shin E, Werkman C, Smith N, Tsuji B, Bulitta J. Periplasmic Target Site Penetration Rates of Two β -lactamase Inhibitors in *Klebsiella Pneumoniae* Carbapenemase-2 (KPC-2) Producing *Klebsiella Pneumoniae* (KP) Characterized by A Novel Assay. ASM Microbe 2022, Online and Washington; June 9-13, 2022.
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 18. Sayed ARM, Elsayed AAS, Shah NR, Sutaria DS, Moya B, **Lang Y**, Shin E, Zhou J, Werkman C, Tsuji BT, Louie A, Drusano GL, and Bulitta JB. Poster. First whole-cell penicillin-binding protein (PBP) binding profiles of carbapenems and cefoxitin in *Klebsiella pneumoniae* (KP) – characterizing the mass balance of penetration and binding in periplasm. ECCMID 2022. Online and Lisbon. Apr 23-26, 2022.
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 30. Zhou J, **Lang Y**, Qian Y, Kim TH, Tao X, Sayed AR, Shin E, Werkman C, Louie A, Drusano GL, Landersdorfer C, Bulitta JB. Thermal stability of β -Lactam antibiotics in broth, agar and water: Precisely achieving target concentrations in vitro by supplement dosing algorithms. ESCMID 2021, Online; July 9-12, 2021.
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32. Werkman C, Shah NR, Lucas D, Oyer J, Megroz M, Sayed AR, Moya B, Wright A, Sutaria DS, Tao X, **Lang Y**, Zhou J, Shin E, Jimenez R, Cadet K, Copik A, Boyce J, Bulitta JB. Synergistic bacterial killing elicited by simultaneous inactivation of Penicillin-Binding Proteins 2 and 3 (PBP2 and PBP3) in a resistance deprived *Acinetobacter baumannii*. ESCMID 2021, Online; July 9-12, 2021.
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